

Global Influenza Surveillance in the U.S. Military

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ABSTRACT

Given that infections caused by various emerging respiratory pathogens and known biological warfare agents often present initially as influenza-like illnesses, there is interest in a near-real-time system that can identify both covert attacks involving biological agents and emerging respiratory pathogens. This article describes an approach integrating the results from lab-based influenza surveillance with several complementary health data streams (outpatient, inpatient, immunization, etc.) to create such an enhanced surveillance system.

1.0 INTRODUCTION

The 1918 influenza pandemic serves as a poignant reminder of how devastating influenza can be. Its ability to generate enormous numbers of casualties, probable travel restrictions, and effects on civilian support infrastructure poses a serious threat to military operations. More recently, in 1996, a United States ship of the line was taken out of service and forced into a foreign port for 2 days while waiting for enough crew members to recover before resuming normal operations.¹ In light of this threat, the U.S. Department of Defense (DoD) maintains a globe-girdling influenza surveillance system, seeking to identify antigenic shifts and drifts at the earliest possible moment. Frighteningly, the threat is not limited to influenza. Emerging infectious diseases such as the Severe Acute Respiratory Syndrome coronavirus and, possibly, biological warfare agents loom ahead. The early stages of many of these infections resemble influenza and are often categorized as influenza-like illnesses (ILI). Given these threats, there has been a concerted effort to adapt existing surveillance systems to provide near-real-time surveillance that could identify covert attacks involving biological agents or the emergence of new respiratory pathogens as well as improve the DoD's capabilities to monitor naturally occurring influenza.

2.0 HISTORY OF INFLUENZA SURVEILLANCE IN THE U.S. MILITARY

Systematic influenza surveillance in the DoD began in 1976 by direction of the USAF Surgeon General. It was called "Project Gargle" to remind people to focus on obtaining throat samples from individuals with ILI. Later, the program expanded to include all of the DoD as part of the Global Emerging Infections Surveillance and Response System (GEIS)² network. The overall program objectives are to:

- Prevent outbreaks from newly emerging viral strains
- Isolate and identify circulating influenza viruses

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- Detect newly emerging subtypes or antigenic drift
- Evaluate influenza vaccine effectiveness

3.0 METHOD

3.1 Population-based Influenza Surveillance

There are two primary components to the DoD Global Influenza Surveillance program. One is a population-based element while the other is etiologically-focused (see 3.2 below). The population-based element, managed by the Naval Health Research Center, San Diego, California, tracks febrile respiratory illness (FRI) incidence rates among basic military trainees³. Trainees merit special attention given their increased risk for respiratory disease outbreaks due to close living conditions, marked physical and psychological stress, and difficulty maintaining personal hygiene under austere training conditions. As a closely monitored and controlled group, they are ideal for surveillance of this type. Medical staff members systematically collect viral specimens (oropharyngeal or nasopharyngeal swabs) from trainees who meet the established case definition. Candidates are those who present for care within 72 hours of symptom onset, have a temperature of more than 100.5° F (38° C), and either a cough, sore throat, or radiographic evidence of a viral pneumonia. These samples then undergo analysis against a viral panel that includes influenza A and B, parainfluenza viruses, respiratory syncytial virus, herpes simplex virus, and adenovirus. This year-round surveillance provides valuable information about current etiologic agents among trainees that in turn helps preventive medicine and public health staff to effectively target their efforts. As the trainees receive a number of vaccines in their first week of training, there is also an opportunity to gather information about vaccine effectiveness.

3.2 Etiologic-based Influenza Surveillance

Etiologic-based surveillance⁴, combined with the population-based component described above, completes the picture. Using the same case definition, the DoD medical staff members at 27 sentinel sites around the globe collect at least six samples each per week during the influenza season (October through April) and submit them to the Air Force Institute for Operational Health (AFIOH)⁵. The sentinel sites are carefully selected to maximize the possibility of capturing specimens of newly emerging viral strains. Thus, a number of the sites are located along the Asia-Pacific Rim since many new strains of influenza have emerged from China in the past. Other sites are major military transportation hubs through which service members routinely pass when returning from duties overseas. Nonsentinel military installations and various DoD overseas research laboratories also submit specimens, especially if there appears to be a respiratory disease outbreak in their area. The Air Force Clinical Reference Laboratory at AFIOH analyzes the samples using the same viral panel described in 3.1. Other DoD laboratories, such as the Naval Health Research Center and US Army Medical Centers, are available to help analyze samples during exceptionally busy seasons. Antigenic subtyping and molecular analysis are performed on a subset of the positive samples. Samples and results are shared with the Centers for Disease Control and Prevention (CDC), who in turn collaborates with the World Health Organization (WHO). This information is a critical component in the decision-making process to determine which strains should be included in the next vaccine, and on some occasions the DoD influenza surveillance program has provided the samples best suited for use as seed viruses in the production process.

4.0 ADAPTING SYSTEMS TO DEAL WITH EMERGING THREATS

Emerging infectious diseases are communicable diseases that have recently become more prevalent or threaten to do so. They can include human, animal, and plant infections. They may be the product of a natural disease outbreak or the result of an attack involving biological agents. Recent examples include Severe Acute Respiratory Syndrome, pulmonary anthrax, and avian flu. It isn't possible to create new surveillance systems for each new disease agent, but it is possible to adapt existing systems. In this case, the goal was to adapt and combine existing systems to provide an enhanced respiratory surveillance program. Available DoD systems included the Electronic Surveillance System for the Early Notification of Community-based Epidemics (ESSENCE), the inpatient data registry, reportable medical events systems, the immunizations databases, trainee FRI surveillance program, and the laboratory influenza surveillance program. Table 1 provides a synopsis of these systems.

DoD System	Description/ Comments
ESSENCE (Electronic Surveillance System for the Early Notification of Community-based Epidemics)	Syndromic surveillance system monitoring categories of outpatient ICD-9 diagnostic codes from primary care clinics and emergency rooms; central DoD repository, updated 1 to 3 times a day
Febrile Respiratory Illness Surveillance	Population-based sampling limited to stateside basic trainees
Influenza Laboratory Surveillance	Convenience sampling at selected sentinel sites; gold standard laboratory confirmation techniques
Inpatient Data Registry	Discharge diagnoses for all hospitalizations; severity-biased with a 30-60 day time lag
Reportable Medical Events	Limited set of selected diagnoses; passive reporting system; only a subset are urgently reportable (within 24 hours), others lag 30-60 days before reaching central DoD repository
Immunizations Data Registry	All immunizations for military and family members; separate systems in each service, but completeness varies, especially with regard to family members

Table 1: Candidate DoD Systems for Use in Enhanced Respiratory Disease Surveillance

4.1 Specific Actions

Given the various shortfalls, no single system in Table 1 could hope to consistently identify emerging outbreaks at the earliest possible moment. Specific enhancements were made to several of the systems to compensate for these limitations.

4.1.1 Modifications to ESSENCE

The core aspect of the DoD ESSENCE is to monitor ambulatory (outpatient) health event data from selected primary care clinics (family practice, pediatrics, and internal medicine), acute care clinics, and emergency

rooms on a daily basis. The system includes data from all of the permanent U.S. military medical treatment facilities around the world, but it does not encompass deployed medical operations. The ICD-9 diagnostic codes were originally mapped against 7 syndromic categories (Respiratory, Fever, Gastrointestinal, Dermatological-Haemorrhagic, Dermatological-Infectious, Neurological, and Coma). The counts of these categories are compared with historical data with alert (between 2 and 3 standard deviations) and alarm (greater than 3 standard deviations) statistical thresholds that trigger investigations. The original system captured influenza illness in the Respiratory and Fever categories. However, the Respiratory category is extremely broad with over 150 ICD-9 codes. Unfortunately, a small number of unusual cases were easily lost against the year-round high background levels of upper respiratory illnesses. To improve the system's ability to capture variations in flu-like illnesses, a new category for Influenza-like Illness (ILI) was created. This category captures cases from the following areas:

- Viral infection
- Acute pharyngitis, laryngitis, tracheitis (or combinations)
- URI of multiple or unspecified sites
- Acute bronchitis, bronchiolitis
- Viral pneumonia
- Influenza-specific diagnoses
- Nonspecific symptoms (fever, throat pain, cough)

4.1.2 Modifications to the Laboratory Influenza Surveillance Program

The primary modification here was to expand the number and placement of sentinel sites. For the first time, the DoD was able to collect viral specimens from American soldiers supporting Operations IRAQI FREEDOM and ENDURING FREEDOM at their deployed locations. This provided samples from geographic areas where previously access had been quite difficult and yet were places where there was a good likelihood of capturing new strains, such as Central Asia. Besides adding new sites, the laboratories increased their capacity and added automatic sequencing equipment to handle the increased sample load. Another enhancement was to compare each positive USAF influenza sample with the USAF immunization database to determine if the individuals had been vaccinated at least 2 weeks prior to the onset of their illness. If so, they were potential breakthrough cases, and this data could be used to focus efforts on possible drift strains that are not good matches with the current vaccine components. Finally, analysis and reporting were performed more frequently, going from weekly to daily during the periods of greatest concern, e.g., during the peak of SARS cases.

4.1.3 Analysis and Interpretation (Bringing the Pieces Together)

The following scenario occurred on a DoD military installation in the fall of 2003 and illustrates how these complementary data sets were used to better assess both the health and operational risks. During the last week of October 2003, the local medical staff began to notice increasing numbers of respiratory disease cases among technical students attending a local course. There were several cases of relatively severe disease that required hospitalization, but not intensive care. Figure 1 shows the ESSENCE Respiratory graph for this time period. Although there is a general upward trend beginning in late October, a statistical threshold was not crossed until 6 November, and then only at the yellow (2 standard deviation) level. Figure 2 shows the Fever curve for the same time period. Here there is a clear cluster of elevations at the red (3 standard deviation) alarm level in the first week of November. Similarly, the percent of all ambulatory visits due to influenza-like

illness jumps precipitously, as shown in Figure 3. Not shown, but also important, was the laboratory influenza surveillance data for samples submitted from sentinel sites in proximity to this installation. These results were overwhelmingly positive for influenza A/Fujian. Although analysts might have been willing to accept the ESSENCE Respiratory category data as a mild seasonal variant, looking at the other data sets convinced them that there was a significant outbreak underway. An investigative team was dispatched and the annual immunization program accelerated to include the remaining base personnel while the outbreak subsided.

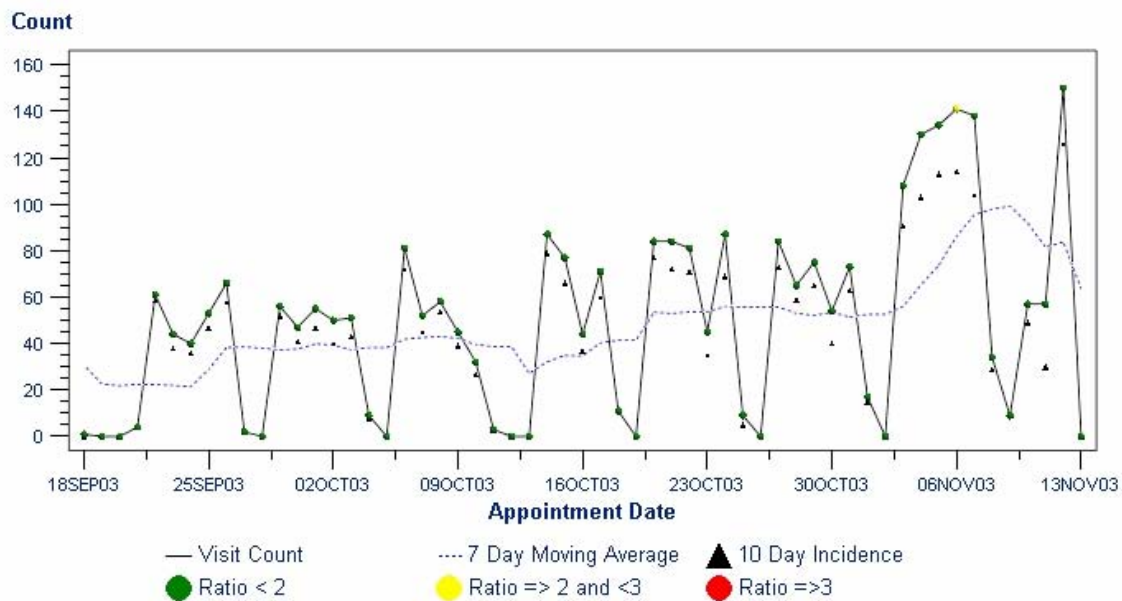


Figure 1: ESSENCE Respiratory Category Graph for Base X

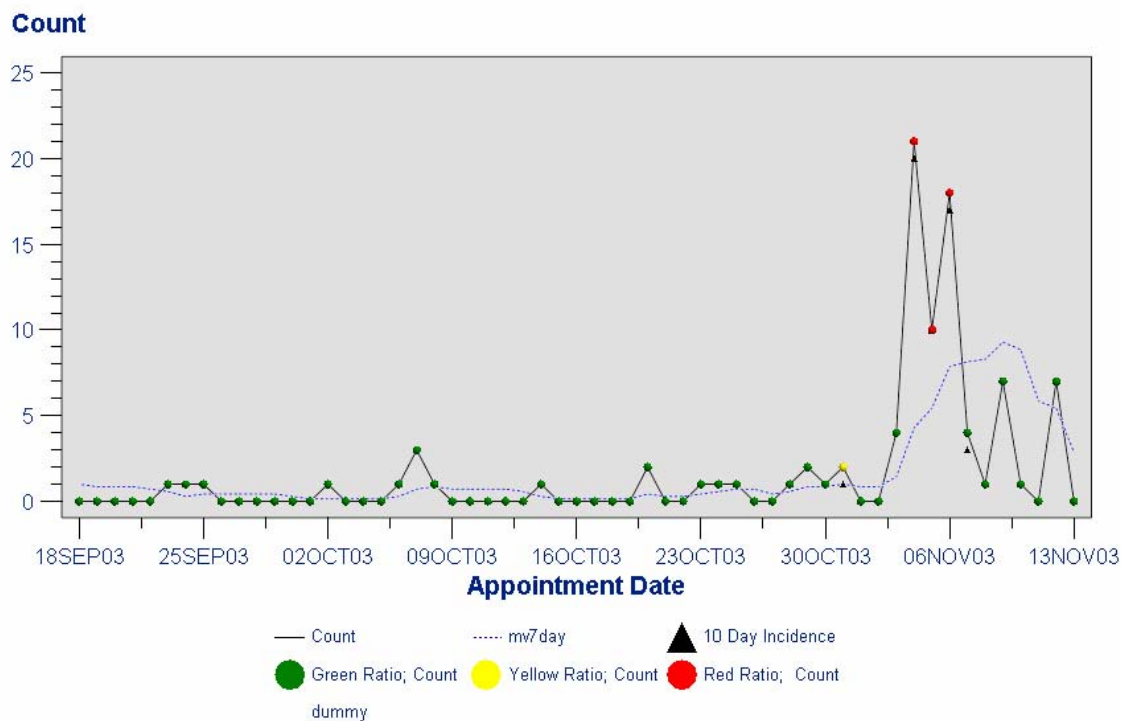


Figure 2: ESSENCE Fever Category Data for Base X

% of Visits for ILI at Base X

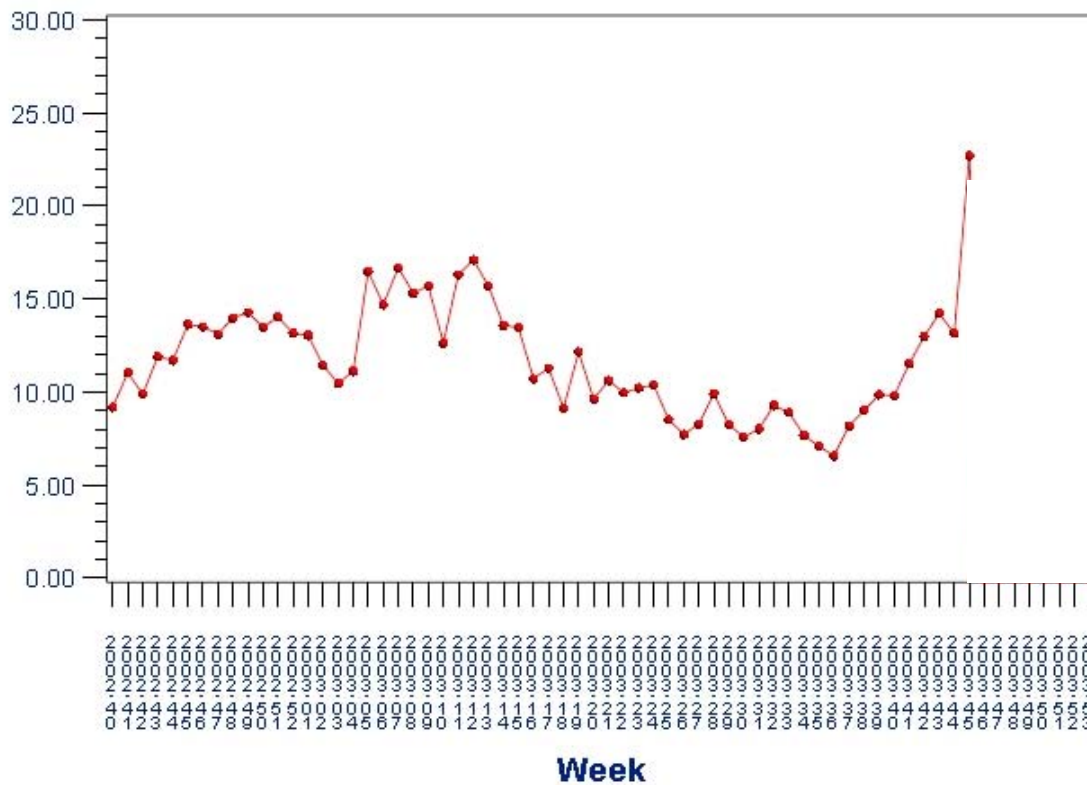


Figure 3: ESSENCE Influenza-like Illness (ILI) Graph for Base X

5. CONCLUSIONS

Emerging infectious diseases and weapons of mass destruction are serious threats to military operations and communities everywhere. Prompt intervention with immunizations, prophylactic medications, or other measures can slow or even stop an outbreak. Such measures are most effective early in the course of the outbreak. Consequently, an active and integrated set of surveillance systems is one of the best ways to stay ahead of biological disease agents. Such integrated and enhanced surveillance systems also may serve as early warning systems for deliberate attacks involving biological agents, though more work is necessary to validate the best types of data and analyses to use for this application.

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- [5] <https://afioh.brooks.af.mil/pestilence/influenza/>

SYMPOSIA DISCUSSION - PAPER 1

Authors Name: Col Cox (US)

Discussor's Name: Dr Reifman (US)

Question:

How does the system compute the threshold to trigger an alert/alarm?

Author's Reply:

It compares the current day's observed count with the mean of the previous six corresponding weekdays. For example, if today is Monday, it compares today's count with the mean of the previous six Mondays.

Yellow Alert = between 2 and 3 standard deviations.

Red alarm = greater than/equal to 3 standard deviations.

Authors Name: Col Cox (US)

Discussor's Name: Dr Foster (US)

Question:

Are the web references in paper generally accessible to NATO military staff?

Author's Reply:

Ref #2: public site

Ref #3: not sure, public, I think

Ref #4: restricted to U.S.A government and military

